REMARKS/ARGUMENTS

Claims 10-14, 17, 19-20, 24-64 are active in this application. Support for Claims 24-64 is found in Claims 1-23. No new matter is added by these amendments.

Applicants wish to thank Examiner Mohamed for the courteous discussion granted to the Applicants' undersigned representative on July 1, 2003. During this discussion the Examiner suggested amendments to focus on, for example, Formulas II and/or IV and/or compounds 1-10. In addition, the method claims for using these compounds were also discussed.

The claims as amended are directed to compounds of Formula II (Claim 10), Formula IV (Claim 17), and a specific formula (Claim 19). All remaining claims are dependent directly to one of these three claims.

Claims 37-52 are directed to methods of antagonizing or agonizing a C5a receptor consistent with the activity of the compound from which the claim depends. These methods are described throughout the specification and data demonstrating efficacy for these activities are presented in Tables 2, 4, 5 and 6 (pages 30, 37, 39 and 41).

Claims 53-64 are drawn to method of treating an inflammatory condition or a method of treating arthritis using the compounds in Claims 10, 17 or 19. These claims are enabled because the Applicants have provided *in vivo* data using well-accepted models for assessing anti-inflammatory and anti-arthritis effects. As stated on page 46, lines 22-25 "many anti-inflammatory drugs currently used in humans were initially evaluated in such assays, and also showed activity in these models of inflammation."

The data are presented in Examples 7 and 8 on pages 45-46. Example 7 demonstrates the inhibition of C5a induced neutropenia *in vivo* using one of the inventive compounds. In addition on page 46, the cyclic antagonists in Table 5 were determined to be active as anti-inflammatory agents in suppressing the onset of either carrageenan-induced paw oedema or

adjuvant-induced polyarthritis. On page 46 the Applicants have also shown in the carrageenan paw oedema assay "that even weak C5a antagonists significantly inhibits development of the oedema after 180 and 270 minutes."

Moreover, in a recent publication by some of the named inventors[1] data are presented which demonstrate the efficacy of compound No. 12 in an antigen-induced arthritis model in the rat. Note that this rat model is a widely used model system for rheumatoid arthritis--see page 2483 column 2, first paragraph which describes the utility of such a rat model. The results of the study demonstrate that compound 12 has a profound effect at inhibiting the action of C5a thereby treating the arthritic condition.

Therefore, in view of the amendments coupled with the data in the specification and the data presented in the attached publication, the claims as presented herein are fully enabled. As a result Applicants request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

[1] Wodruff et al, Arthritis and Rheumatism, vol. 46 No. 9, September 2002.

Applicants further request that this application now be passed to issuance.

Respectfully submitted,

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